IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF **YUPING QIU, ET AL**
FOR: **PYRAZOLOPURINE- BASED TRICYCLIC COMPOUNDS AND PHARMACEUTICAL COMPOSITIONS COMPRISING SAME**
APPLICATION NO: **10/785612** APPLICATION DATE: **02/24/2004**
ART UNIT: **1624** EXAMINER: **LEESER, ERICH A**
CONFIRMATION NO: **2956** USPTO CUSTOMER NO: **23914**

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Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE AFTER FINAL REJECTION

Sir:

This response is being submitted in reply to the Office Action dated July 3, 2007.

Reconsideration and reexamination is respectfully requested. The indication of allowable subject matter is acknowledged with appreciation.

The Examiner had previously rejected claims 1-5 and 16 as being unpatentable over Ikesu et al. Applicants amended claims in such a way as they believed that the reference would be avoided. However, the Examiner has maintained the rejection against these claims. Applicants' continue to traverse this rejection.

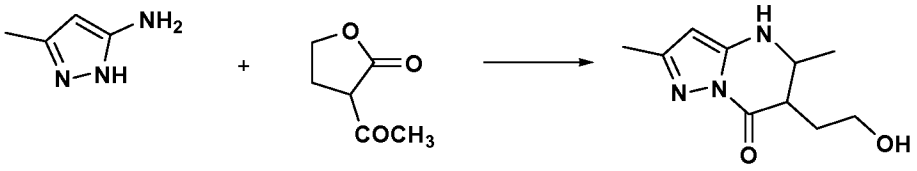
First, Applicant's assert that the Ikesu et al. reference is not analogous art. In order to rely on a reference under Section 103, the reference must be analogous art. "in order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." See MPEP 2141.01(a). Additionally, "similarities and differences in structure and function of the inventions . . . carry far greater weight." MPEP 2141.01(a) The instant application is directed to compounds which are inhibitors of IKK. Such inhibitors are useful in the treatment of diseases. By contrast, Ikesu et al. discloses compounds which are useful as photographic couplers. While both the Ikesu et al. reference and the instant application are directed to compounds, the use of photographic couplers can not be said to be

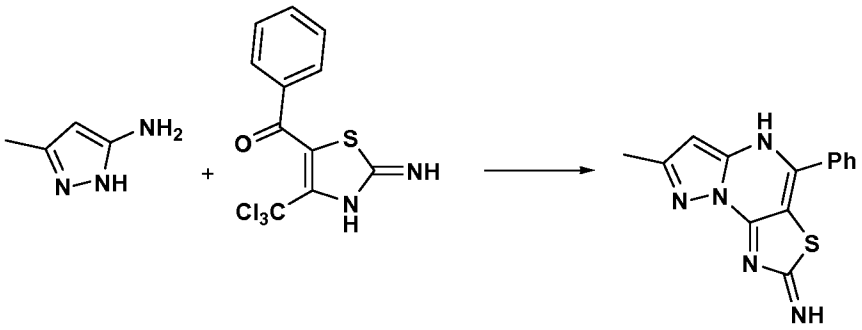
within the same field of endeavor nor is it pertinent to the particular problem concerning the inventor in the instant invention. In deciding what compounds would be useful for the inhibition of IKK and therefore the treatment of diseases, one would not be drawn to the field of photographic couplers.

Additionally, the prior art compounds should share the same utility as the claimed compounds. The premise underlying the motivation to modify the prior art compound to structurally similar compounds derives from the expectation of one skilled in the art that such compounds will have similar properties. In the instant situation, the motivation to modify the compounds of the Ikesu et al. reference would be to arrive at other photographic couplers. There is no motivation within Ikesu et al. to modify the compounds described therein in such a way as to arrive at IKK inhibitors which are useful for treating disease.

Furthermore, one of skill in the art would not be led by the reference to make the changes to arrive at the structures as described in the instant application. In the Ikesu et al. reference, the compound of column 5, fifth structure is not the same heterocycle as described in the instant application. The structure is a di-hydro heterocycle and there is no teaching within the reference of how one would take that structure and convert it into the compounds as described in the instant application. Additionally, the compound in column 11, fourth structure down, discloses a compound that appears to be closer to the core structure of the instant application. However, as is evident, there are mistakes made in the rendering of this structure and it is not entirely clear what the reference is disclosing. Additionally, by looking at this structure alone and as a whole (which is not disclosed generically elsewhere in the reference), there is no teaching of this core structure having the substitution pattern as described in the instant application, that is the substitution in the instant application provides for $-NR_3R_4$ on the 6 membered ring. The compound in column 11 only teaches $-C_{12}H_{25}$ substitution on the 6-membered ring.

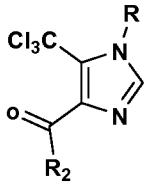
Finally, the Ikesu et al. reference is not an enabling disclosure which would enable the preparation of the compounds of either the Ikesu et al. reference (which are being relied upon in the rejection of the instant application) or of the compounds of the instant application. Ikesu et al. describes the synthesis of compounds 1 and 18. Neither of these preparations show how to prepare a compound containing an imidazole ring as a part of the tricyclic system as described in the instant application. Additionally, neither of these references describe the formation of the central 6-membered ring having a $-NR_3R_4$ substituent. Both of these syntheses describe the condensation of a substituted-keto-heterocycle with 3-amino-5-methylpyrazole as shown below:



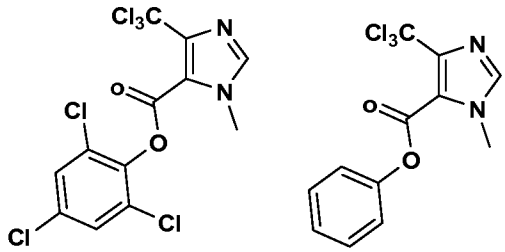


Neither of these procedures describe a method of preparing the compounds which are being used in the instant rejection or the compounds which are disclosed in the instant application, that is to say, a compound having the core structure with a imidazole, with a substituent off of the imidazole ring as described and the substituent -NR_3R_4 off of the central 6-membered ring.

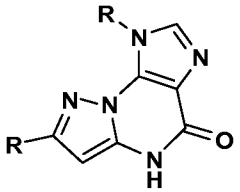
To prepare the compounds of Ikesu which are being relied upon in the instant rejection, one would presumably need to start with the following starting materials:



A search of Chem Abstracts found two similar imidazoles of the following structure:



It is presumed that the cyclization of these intermediates would result in the following lactam (it is unknown if there is actual teaching of this cyclization):



However, the search did not find any imidazoles having the alkyl ketone present such as would be needed to prepare the compound described in Ikesu et al. Therefore, the starting materials to prepare these heterocycles were not known and therefore the preparation of the compounds is not enabled. In addition to not being able to prepare the compounds as disclosed in Ikesu et al., there is not an enabling disclosure within the Ikesu et al. reference of how to make the compounds of the instant invention having imidazole ring as part of the tricyclic system and the $-NR_3R_4$ substituent on the 6-membered ring.

Claim 16 was rejected for being obvious over Ikesu et al. The Office Action dated January 22, 2007 states that pharmaceutical compositions which use pharmaceutically acceptable carrier can be found at steps 2 and 3. It goes on to say that "Pharmaceutical compositions of the compounds of the prior art render the instant compounds obvious because Applicant discloses that the inventions compounds are suitable for pharmaceutically acceptable compositions." First, the information described in steps 2 and 3 are the synthesis of intermediates of a different heterocycle. They do not describe the preparation of a compound that would render the instant application obvious. It merely describes the synthesis of these intermediates. Also, these steps describe sequences in running a reaction. The mere presence of water in a reaction mixture in the synthesis of an intermediate does not render a pharmaceutical composition obvious. Secondly, the use of Applicant's disclosure that the compounds of the instant application are suitable for pharmaceutically acceptable compositions is impermissible hindsight. An invention may not be rendered obvious by the use of its own disclosure.

In summary, it is believed that the instant invention is not obvious over the Ikesu et al. reference. One of skill in the art, would first have to decide to look at the Ikesu et al reference as a starting point for making IKK inhibitors, would then have to decide what changes to make to the Ikesu et al. compounds which are photographic couplers to arrive at IKK inhibitors which are useful for treating disease, and then have to develop a synthesis of these compounds. None of these tasks are obvious based on the Ikesu et al reference. Therefore, withdrawal of the Section 103 reference is respectfully requested.

The application is believed to be in condition for allowance and notification thereof is respectfully requested. The Examiner is welcomed to call Applicants' representative at the telephone number below if he feels a telephone interview would further prosecution of this invention.

Respectfully submitted,

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Date: September 4, 2007

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